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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/762,588      | 01/21/2004  | Grigoriy S. Tchaga   | CLON-056US2         | 3721             |

24353 7590 11/27/2006

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EXAMINER

ROOKE, AGNES BEATA

ART UNIT PAPER NUMBER

1656

DATE MAILED: 11/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action  
Before the Filing of an Appeal Brief**

Application No.

10/762,588

Applicant(s)

TCHAGA ET AL.

Examiner

Agnes B. Rooke

Art Unit

1653

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 03 October 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 6 months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

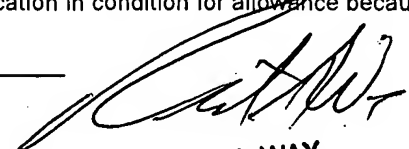
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
The status of the claim(s) is (or will be) as follows:  
Claim(s) allowed: \_\_\_\_\_.  
Claim(s) objected to: \_\_\_\_\_.  
Claim(s) rejected: 11-13, 16, 18021, 23, 24.  
Claim(s) withdrawn from consideration: \_\_\_\_\_.

**AFFIDAVIT OR OTHER EVIDENCE**

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.  
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_  
13. ☐ Other: \_\_\_\_\_.

  
**ROBERT A. WAX  
PRIMARY EXAMINER**

Continuation of 11. does NOT place the application in condition for allowance because: Claims 11-13, 16, 18-21, 23-24 stand rejected under 35 U.S.C. 103(a), because the prior art over Tchaga in view of Porath still applies.

Applicants state that while both methods in the prior art are broadly directed to "purifying a protein of interest," Tchaga method applies to tagged proteins only, and that Porath method applies to untagged proteins (native proteins) only. Also, Applicants state that there is no reason to expect that a method directed to the purification of untagged proteins would provide an improvement in the purification of ion binding-tagged proteins.

Examiner disagrees and states that the prior art is applicable for all the arguments mentioned in the Final office action. Further, examiner states that it is known in the prior art that affinity chromatography that utilizes metal binding, incorporates a common technique that involves engineering a sequence of 6 to 8 histidines into the C-terminal of the protein, where the polyhistidine binds strongly to divalent metal ions, particularly nickel. The protein can be passed through a column containing immobilized nickel ions, which binds polyhistidine tag. While this procedure is generally used for the purification of recombinant proteins with an engineered affinity tag (such as 6xhis tag), it can also be used for natural proteins with an inherent affinity for divalent cations.

Next, Applicants state that examiner does not present any support for the statement that "purification of proteins usually occurs in the presence of different columns...and the use of additional columns or different ions in the protocol is dictated by the need to optimize the conditions for the most efficient and maximum recovery of the protein of interest..." Further, Applicants state that the tagged status of the protein is relevant.

Examiner disagrees, and states that the protein purification utilizes different columns and different buffers in order to purify a protein of interest, and that in the the purification process, a choice of a column or a buffer depends on the protein's size, physico-chemical property and binding affinity. Also, examiner agrees that the tagged status of the protein is relevant because it will dictate a proper choice of a column and a buffer (i.e. for tagged proteins a column with immobilized nickel ions in a resin is most appropriate, for example).

Moreover, Applicants state that there is no motivation to combine the prior art references. Examiner would like to point out that according to the MPEP 2143.02, regarding the obviousness rejection, only a reasonable expectation of success is required and that according to MPEP 2144, the rationale to modify or combine the prior art does not have to be expressly stated in the prior art; the rationale may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art, or established scientific principles, for example.

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